

## Web materials

**Web Table 1.** Definition of socio-economic status per study, and information on day-care and infections available for each study, Childhood Leukemia International Consortium

First author, Year (Reference No.)	Study	Indicator used for definition of socio-economic status	Information on day-care	Sites of common infection	Frequency (for each site)
Milne, 2009 (1)	AUS_ALL	Family annual income at diagnosis (Low: ≤ \$40000; Medium: \$40001-\$70000; High: ≥ \$70000)	For each year of age: average number of children in the group, average number of hours per week at day-care, and duration of day-care attendance.	No data	-
Infante-Rivard, 2005 (2)	CA_QCLS	Family annual income at diagnosis (Low: ≤ \$10000; Medium: \$10000-\$39999; High: ≥ \$40000)	Day nursery attendance with average number of hours per week and age at start.	No data	-
Clavel, 2005 (3)	FR_ADELE	Higher of maternal and paternal job categories at the time of diagnosis/interview (Low: "Factory and agricultural workers, unemployed"; Medium: "Administrative, sales and service workers"; High: "Intellectual/scientific jobs, manager and intermediate professions")	Full-time day-care center attendance ('crèche'); part-time day-care center attendance ('halte-garderie'); Child minder. Age at start for each type of day-care.	Any infection	None, <1 per trimester, ≥ 1/trimester, ≥ 1/ month
Jourdan-Da Silva, 2004 (4)	FR_ELECTRE	Higher of maternal and paternal job categories at the time of diagnosis/interview (Low: "Factory and agricultural workers, unemployed"; Medium: "Administrative, sales and service workers"; High: "Intellectual/scientific jobs, manager and intermediate professions")	Full-time day-care center attendance ('crèche'); part-time day-care center attendance ('halte-garderie'); Child minder. Age at start for each type of day-care.	Ear Nose Throat infection, gastroenteritis, any other	None, <1 per trimester, ≥ 1/trimester, ≥ 1/ month
Rudant, 2010 (5)	FR_ESCALE	Higher of maternal and paternal job categories at the time of diagnosis/interview (Low: "Factory and agricultural workers, unemployed"; Medium: "Administrative, sales and service workers"; High: "Intellectual/scientific jobs, manager and	Full-time day-care center attendance ('crèche'); part-time day-care center attendance ('halte-garderie'); Child minder. Age at start for each type of day-care.	Tonsillitis, otitis, upper respiratory tract infections, bronchiolitis and other lower respiratory tract infections, Gastroenteritis, urinary	None, between 1 and 3, 4 or more

		"intermediate professions")			
Petridou, 2008 (6)	GR_NARECHEM	Higher of maternal and paternal levels of education (Low: secondary education not completed; Medium: secondary education completed; High: Tertiary education)	Day-care center attendance with age at start.	Ear Nose Throat infection, gastroenteritis, pneumonia, bronchiolitis, Urinary, others	number of episodes
Magnani, 2014 (7)	IT_SETIL	Higher of maternal and paternal levels of education (Low: secondary education not completed; Medium: secondary education completed; High: Tertiary education)	Full-time day-care center attendance or part-time day-care center attendance, age at start and number of children in the class.	Pneumonia, bronchiolitis, urinary, other	number of episodes
Dockerty, 1999 (8)	NZ_NZCCS	Higher of maternal and paternal social classes	Day nursery or community group attendance (play, mother & toddler club, tumble tot, ...); child minder. For each type of day-care: average number of children, average number of day sessions per week, age at start.	Ear, mouth, gastroenteritis, cold, persistent cough, other	None, 1 or more
Roman, 2007 (9)	UK_UKCCS	Deprivation index in tertiles (address at diagnosis).	Day nursery or community group attendance (play, mother & toddler, club, tumble tot, ...); child minder. For each type of day-care: average number of children, average number of half-day sessions per week, age at start.	Ear Nose Throat infection, gastroenteritis, any other	number of episodes
Zierhut, 2012 (10)	US_COG15	Annual Household Income (Low: ≤ \$19000; Medium: \$20000-\$39999; High: ≥ \$40000)	Day nursery attendance with average number of hours per week and age at start.	No data	
Bartley, 2010 (11)	US_NCCLS	Annual Household Income (Low: ≤ \$30000; Medium: \$30000-\$74999; High: ≥ \$75000)	Average number of children and average number of hours per week at day-care, age at start day-care.	Ear, mouth, diarrhea, cold, persistent cough, other	number of episodes

AUS\_ALL: Australian study of causes of acute lymphoblastic leukaemia in children; CA\_QCLS: Quebec childhood leukemia study (Canada); FR\_ADELE: Adele study (France); FR\_ELECTRE: Electre study (France); FR\_ESCALE: Epidemiological study on childhood cancer and leukemia (France); GR\_NARECHEM: Nationwide registration for childhood haematological malignancies (Greece); IT\_SETIL: Study on the etiology of childhood lymphohematopoietic malignancies (Italy); NZ\_NZCCS: New Zealand childhood cancer study; UK\_UKCCS: United Kingdom childhood cancer study; US\_COG15: Children's oncology group study (US); US\_NCCLS: Northern California childhood leukemia study (US).

**Web Table 2.** Description of the exposure of interest among controls (controls aged two years and over from all studies combined)

	Maternal education			Socioeconomic status			Birth order		Day-care center attendance		Breastfeeding		
	Not secondary	Secondary	Tertiary	Low	Medium	High	1	≥ 2	No	Yes	No	1-5 months	≥ 6 months
	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
<b>Breastfeeding</b>													
No breastfeeding	54%	36%	19%	45%	37%	26%	32%	37%	37%	25%			
1 to 5 months	32%	40%	43%	35%	38%	44%	43%	36%	38%	45%			
≥ 6 months	14%	24%	38%	20%	25%	30%	25%	27%	25%	30%			
p-value ( $\chi^2$ test)		<0.0001			<0.0001			<0.0001		<0.0001			
<b>Day-care center attendance</b>													
No	89%	81%	73%	86%	80%	72%	79%	81%					
Yes	11%	19%	27%	14%	20%	28%	21%	19%					
p-value ( $\chi^2$ test)		<0.0001			<0.0001			0.001					
<b>Early common infections</b>													
No	34%	34%	34%	36%	35%	33%	35%	33%	38%	21%	31%	34%	39%
Yes	66%	66%	66%	64%	65%	67%	65%	67%	62%	79%	69%	66%	61%
p-value ( $\chi^2$ test)		0.89			0.11			0.10		<0.0001		<0.0001	

**Web Table 3.** Association between ALL and birth order, day-care, breastfeeding and common infections in the first year of life: pooled stratified analyses of 11 studies, restricted to children aged  $\geq 2$  years, Childhood Leukemia International Consortium.

Strata	Birth order		Day-care center		Breastfeeding		Common infection			
	$(\geq 2 \text{ vs. } 1)$		$(\text{yes vs. no})$		$(\geq 6 \text{ months vs. no})$		$(\geq 1 \text{ vs. none})^b$		$(\geq 4 \text{ vs. none})^c$	
	OR <sup>a</sup>	95%CI	OR <sup>a</sup>	95%CI	OR <sup>a</sup>	95%CI	OR <sup>a</sup>	95%CI	OR <sup>a</sup>	95%CI
<b>By birth order</b>										
Birth order 1			<b>0.74</b>	0.65, 0.84	<b>0.83</b>	0.73, 0.94	<b>0.98</b>	0.87, 1.12	<b>0.90</b>	0.76, 1.07
Birth order $\geq 2$			<b>0.78</b>	0.70, 0.89	<b>0.95</b>	0.82, 1.10	<b>0.93</b>	0.82, 1.04	<b>0.92</b>	0.79, 1.08
				$p_{int}=0.91$		$p_{int}=0.78$		$p_{int}=0.12$		$p_{int}=0.61$
<b>By day-care center attendance &lt;1 year old</b>										
No day-care center attendance	<b>0.92</b>	0.86, 0.99			<b>0.88</b>	0.80, 0.97	<b>0.97</b>	0.88, 1.06	<b>0.89</b>	0.78, 1.00
Day-care center attendance	<b>0.97</b>	0.82, 1.13			<b>0.85</b>	0.68, 1.07	<b>0.96</b>	0.76, 1.21	<b>0.97</b>	0.74, 1.27
			$p_{int}=0.91$			$p_{int}=0.39$		$p_{int}=0.81$		$p_{int}=0.71$
<b>By breastfeeding</b>										
No breastfeeding	<b>0.95</b>	0.85, 1.06	<b>0.83</b>	0.71, 0.98			<b>1.09</b>	0.93, 1.27	<b>0.91</b>	0.76, 1.10
< 6 months	<b>0.91</b>	0.82, 1.01	<b>0.71</b>	0.62, 0.81			<b>0.84</b>	0.74, 0.96	<b>0.78</b>	0.66, 0.92
$\geq 6$ months	<b>0.99</b>	0.87, 1.13	<b>0.78</b>	0.66, 0.92			<b>0.95</b>	0.79, 1.13	<b>1.01</b>	0.78, 1.30
		$p_{int}=0.57$		$p_{int}=0.11$				$p_{int}=0.05$		$p_{int}=0.54$
<b>By common infection &lt;1 year old<sup>a</sup></b>										
None	<b>0.95</b>	0.83, 1.08	<b>0.74</b>	0.59, 0.92	<b>1.04</b>	0.87, 1.24				
At least one	<b>0.84</b>	0.76, 0.93	<b>0.74</b>	0.66, 0.84	<b>0.86</b>	0.75, 0.99				
		$p_{int}=0.14$		$p_{int}=0.81$		$p_{int}=0.10$				

ALL: acute lymphoblastic leukemia, CI: confidence interval, OR: odds ratios;  $p_{int}$ : p-value for interaction

<sup>a</sup> pooled OR and 95%CI estimated by unconditional logistic models adjusted for age, gender, study center, maternal education and maternal age at child's birth.

<sup>b</sup> 8 studies: FR\_ADELE, FR\_ELECTRE, FR\_ESCALE, GR\_NARECHEM, IT\_SETIL, NZ\_NZCCS, UK\_UKCCS, US\_NCCLS

<sup>c</sup> 7 studies: FR\_ADELE, FR\_ELECTRE, FR\_ESCALE, GR\_NARECHEM, IT\_SETIL, UK\_UKCCS, US\_NCCLS

**Web Table 4.** Association between ALL and breastfeeding, birth order, day-care and history of early common infections: pooled analysis of 11 studies by ALL subtypes and by age, restricted to children aged  $\geq 2$  years, Childhood Leukemia International Consortium.

	ALL subtype 2-14 years old						B cell ALL					
	B cell ALL			T cell ALL			2-5 years old			6-14 years old		
	N=5852	OR <sup>a</sup>	95%CI	N=803	OR <sup>a</sup>	95%CI	N=3849	OR <sup>a</sup>	95%CI	N=2003	OR <sup>a</sup>	95%CI
<b>Breastfeeding</b>												
No	2078	<b>1.00</b>	Ref.	296	<b>1.00</b>	Ref.	1352	<b>1.00</b>	Ref.	726	<b>1.00</b>	Ref.
Yes	3725	<b>0.96</b>	0.89, 1.03	499	<b>0.96</b>	0.82, 1.13	2471	<b>0.96</b>	0.88, 1.05	1254	<b>0.97</b>	0.86, 1.09
< 6 months	2368	<b>1.02</b>	0.94, 1.10	303	<b>0.98</b>	0.82, 1.17	1553	<b>1.01</b>	0.92, 1.12	815	<b>1.05</b>	0.92, 1.19
$\geq 6$ months	1338	<b>0.86</b>	0.78, 0.94	193	<b>0.94</b>	0.77, 1.16	906	<b>0.88</b>	0.78, 0.98	432	<b>0.83</b>	0.71, 0.97
<b>Breastfeeding duration</b>												
No breastfeeding	2078	<b>1.00</b>	Ref.	296	<b>1.00</b>	Ref.	1352	<b>1.00</b>	Ref.	726	<b>1.00</b>	Ref.
1 month or less	1080	<b>1.07</b>	0.97, 1.18	132	<b>1.02</b>	0.82, 1.27	714	<b>1.06</b>	0.94, 1.20	366	<b>1.11</b>	0.94, 1.30
2-4 months	1045	<b>1.00</b>	0.91, 1.11	135	<b>0.94</b>	0.75, 1.17	679	<b>1.01</b>	0.89, 1.14	366	<b>1.01</b>	0.86, 1.19
5-7 months	636	<b>0.91</b>	0.82, 1.02	93	<b>1.01</b>	0.78, 1.29	407	<b>0.87</b>	0.75, 1.01	229	<b>1.01</b>	0.84, 1.21
8-10 months	336	<b>0.77</b>	0.67, 0.89	46	<b>0.76</b>	0.54, 1.06	233	<b>0.80</b>	0.67, 0.96	103	<b>0.72</b>	0.56, 0.92
11-13 months	311	<b>0.83</b>	0.71, 0.97	44	<b>0.92</b>	0.65, 1.30	206	<b>0.85</b>	0.70, 1.03	105	<b>0.80</b>	0.62, 1.03
14 months and more	297	<b>0.89</b>	0.76, 1.04	46	<b>1.15</b>	0.86, 1.62	220	<b>0.98</b>	0.81, 1.19	77	<b>0.69</b>	0.52, 0.92
<b>Birth order</b>												
1	2716	<b>1.00</b>	Ref.	350	<b>1.00</b>	Ref.	1782	<b>1.00</b>	Ref.	934	<b>1.00</b>	Ref.
2 and more	3088	<b>0.93</b>	0.87, 0.99	443	<b>1.03</b>	0.88, 1.20	2043	<b>0.97</b>	0.89, 1.06	1045	<b>0.86</b>	0.77, 0.97
2	1970	<b>0.94</b>	0.87, 1.01	275	<b>1.00</b>	0.84, 1.19	1295	<b>0.98</b>	0.89, 1.07	675	<b>0.87</b>	0.77, 0.99
3	769	<b>0.93</b>	0.83, 1.03	118	<b>1.12</b>	0.88, 1.41	523	<b>0.98</b>	0.86, 1.12	246	<b>0.83</b>	0.70, 0.99
4	224	<b>0.82</b>	0.69, 0.98	31	<b>0.99</b>	0.66, 1.48	156	<b>0.89</b>	0.71, 1.10	68	<b>0.71</b>	0.52, 0.95
5	69	<b>0.87</b>	0.65, 1.18	11	<b>1.10</b>	0.58, 2.11	40	<b>0.75</b>	0.51, 1.12	29	<b>1.08</b>	0.68, 1.74
$\geq 6$	56	<b>0.96</b>	0.68, 1.35	8	<b>1.21</b>	0.57, 2.59	29	<b>0.78</b>	0.49, 1.24	27	<b>1.21</b>	0.72, 2.01
<b>Day-care center attendance &lt; 1 year old</b>												
No day-care center	4865	<b>1.00</b>	Ref.	679	<b>1.00</b>	Ref.	3166	<b>1.00</b>	Ref.	1699	<b>1.00</b>	Ref.
Day-care center	804	<b>0.76</b>	0.69, 0.84	100	<b>0.76</b>	0.61, 0.96	562	<b>0.74</b>	0.66, 0.83	242	<b>0.82</b>	0.69, 0.96
<b>Frequency</b>												
Part-time	447	<b>0.75</b>	0.66, 0.85	58	<b>0.83</b>	0.61, 1.12	307	<b>0.71</b>	0.61, 0.83	140	<b>0.85</b>	0.68, 1.05
Full-time	344	<b>0.78</b>	0.68, 0.89	40	<b>0.68</b>	0.49, 0.96	246	<b>0.77</b>	0.65, 0.91	98	<b>0.79</b>	0.62, 1.02

### **Age at start of day-care center attendance**

≥ 24 months or never	4155	<b>1.00</b>	Ref.	609	<b>1.00</b>	Ref.	2679	<b>1.00</b>	Ref.	1476	<b>1.00</b>	Ref.
14-23 months	322	<b>1.04</b>	0.90, 1.20	33	<b>0.82</b>	0.57, 1.18	240	<b>1.01</b>	0.85, 1.20	82	<b>1.09</b>	0.83, 1.44
11-13 months	166	<b>0.96</b>	0.79, 1.16	15	<b>0.67</b>	0.40, 1.15	111	<b>0.84</b>	0.67, 1.07	55	<b>1.27</b>	0.91, 1.77
8-10 months	132	<b>0.77</b>	0.62, 0.95	18	<b>0.81</b>	0.50, 1.33	91	<b>0.73</b>	0.57, 0.94	41	<b>0.86</b>	0.59, 1.24
5-7 months	188	<b>0.80</b>	0.67, 0.95	22	<b>0.70</b>	0.45, 1.09	125	<b>0.74</b>	0.59, 0.92	63	<b>0.91</b>	0.68, 1.24
0-4 months	392	<b>0.75</b>	0.66, 0.85	49	<b>0.70</b>	0.51, 0.96	285	<b>0.75</b>	0.64, 0.87	107	<b>0.75</b>	0.59, 0.94

### **Any day-care < 1 year old**

No day-care	1307	<b>1.00</b>	Ref.	185	<b>1.00</b>	Ref.	836	<b>1.00</b>	Ref.	471	<b>1.00</b>	Ref.
Child minder	339	<b>1.02</b>	0.87, 1.19	50	<b>1.02</b>	0.71, 1.45	224	<b>1.02</b>	0.83, 1.24	115	<b>1.04</b>	0.80, 1.34
Day-care center	402	<b>0.72</b>	0.63, 0.83	48	<b>0.64</b>	0.45, 0.90	285	<b>0.74</b>	0.62, 0.87	117	<b>0.70</b>	0.55, 0.89

## Common infections in the first year of life

None	1460	<b>1.00</b>	Ref.	196	<b>1.00</b>	Ref.	884	<b>1.00</b>	Ref.	576	<b>1.00</b>	Ref.
1 or more	2297	<b>0.94</b>	0.86, 1.03	308	<b>0.99</b>	0.80, 1.22	1586	<b>0.97</b>	0.86, 1.09	711	<b>0.91</b>	0.79, 1.06

#### **Number of common infections in the first year of life**

None	1453	<b>1.00</b>	Ref.	195	<b>1.00</b>	Ref.	875	<b>1.00</b>	Ref.	578	<b>1.00</b>	Ref.
1 to 3	1433	<b>0.96</b>	0.87, 1.06	206	<b>1.07</b>	0.86, 1.34	984	<b>1.01</b>	0.89, 1.14	449	<b>0.90</b>	0.77, 1.06
4 or more	792	<b>0.89</b>	0.79, 1.00	94	<b>0.81</b>	0.62, 1.08	547	<b>0.90</b>	0.77, 1.04	245	<b>0.89</b>	0.74, 1.08

### **Specific sites of infection**

Ear nose throat

None	1662	<b>1.00</b>	Ref.	209	<b>1.00</b>	Ref.	1027	<b>1.00</b>	Ref.	635	<b>1.00</b>	Ref.
1 to 3	1033	<b>1.00</b>	0.91, 1.11	138	<b>1.12</b>	0.88, 1.43	702	<b>1.02</b>	0.90, 1.17	331	<b>0.97</b>	0.82, 1.15
4 or more	433	<b>0.91</b>	0.79, 1.05	46	<b>0.78</b>	0.55, 1.12	290	<b>0.91</b>	0.76, 1.09	143	<b>0.90</b>	0.71, 1.13

Otitis

<b>Units</b>	<b>N</b>	<b>M</b>	<b>S.E.</b>	<b>Ref.</b>												
None	746	<b>1.00</b>		Ref.	79	<b>1.00</b>		Ref.	485	<b>1.00</b>		Ref.	261	<b>1.00</b>		Ref.
1 to 3	290	<b>0.94</b>		0.79, 1.12	40	<b>1.27</b>		0.84, 1.92	192	<b>0.98</b>		0.78, 1.22	98	<b>0.90</b>		0.68, 1.20
4 or more	110	<b>0.91</b>		0.71, 1.17	8	<b>0.55</b>		0.26, 1.16	62	<b>0.78</b>		0.57, 1.09	48	<b>1.05</b>		0.72, 1.53

#### **Lower respiratory tract infection**

	None	1794	1.00	Ref.	223	1.00	Ref.	1114	1.00	Ref.	680	1.00	Ref.
1 to 3		359	0.88	0.75, 1.03	63	1.04	0.74, 1.46	263	0.97	0.80, 1.18	96	0.69	0.52, 0.91
4 or more		82	0.71	0.54, 0.92	12	0.54	0.28, 1.02	66	0.73	0.53, 1.01	26	0.66	0.41, 1.06

#### **4 or more Gastric antacids**

Gastroenteritis      8715 - 1.00      Ref.      353 - 1.00      Ref.      1716 - 1.00      Ref.      869 - 1.00      Ref.

1 to 3	382	<b>0.96</b>	0.84, 1.09	32	<b>0.67</b>	0.46, 0.98	252	<b>0.86</b>	0.73, 1.02	130	<b>1.16</b>	0.93, 1.45
4 or more	38	<b>0.79</b>	0.54, 1.16	10	<b>1.74</b>	0.88, 3.43	28	<b>0.82</b>	0.52, 1.30	10	<b>0.71</b>	0.35, 1.45

ALL: acute lymphoblastic leukemia, CI: confidence interval, OR: odds ratios;

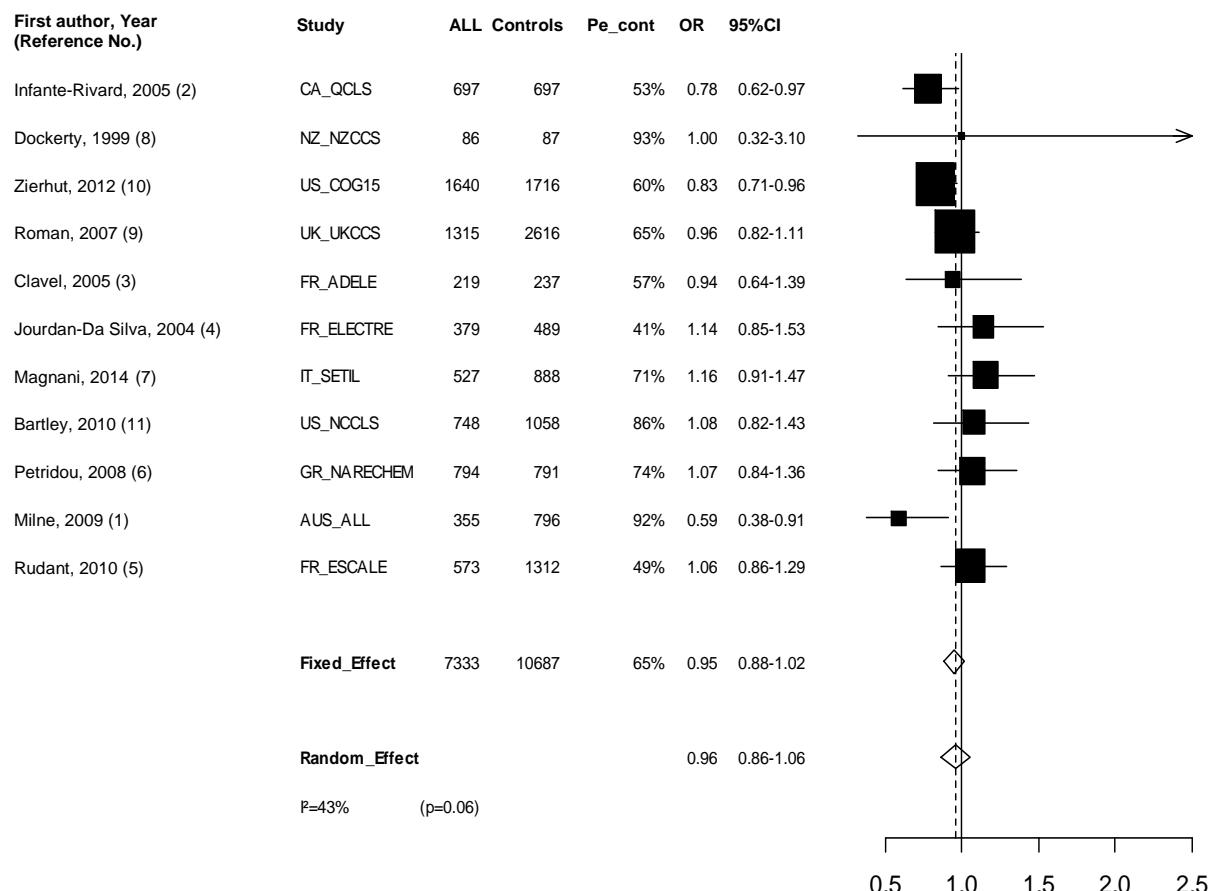
<sup>a</sup> pooled OR and 95%CI estimated by unconditional logistic models adjusted for age, gender, study center, maternal education and maternal age at child's birth.

**Web Figure 1. Association between ALL and breastfeeding**, restriction to children aged  $\geq 2$  years, meta-analysis of 11 studies, Childhood Leukemia International Consortium. Studies are ordered by increasing study period.

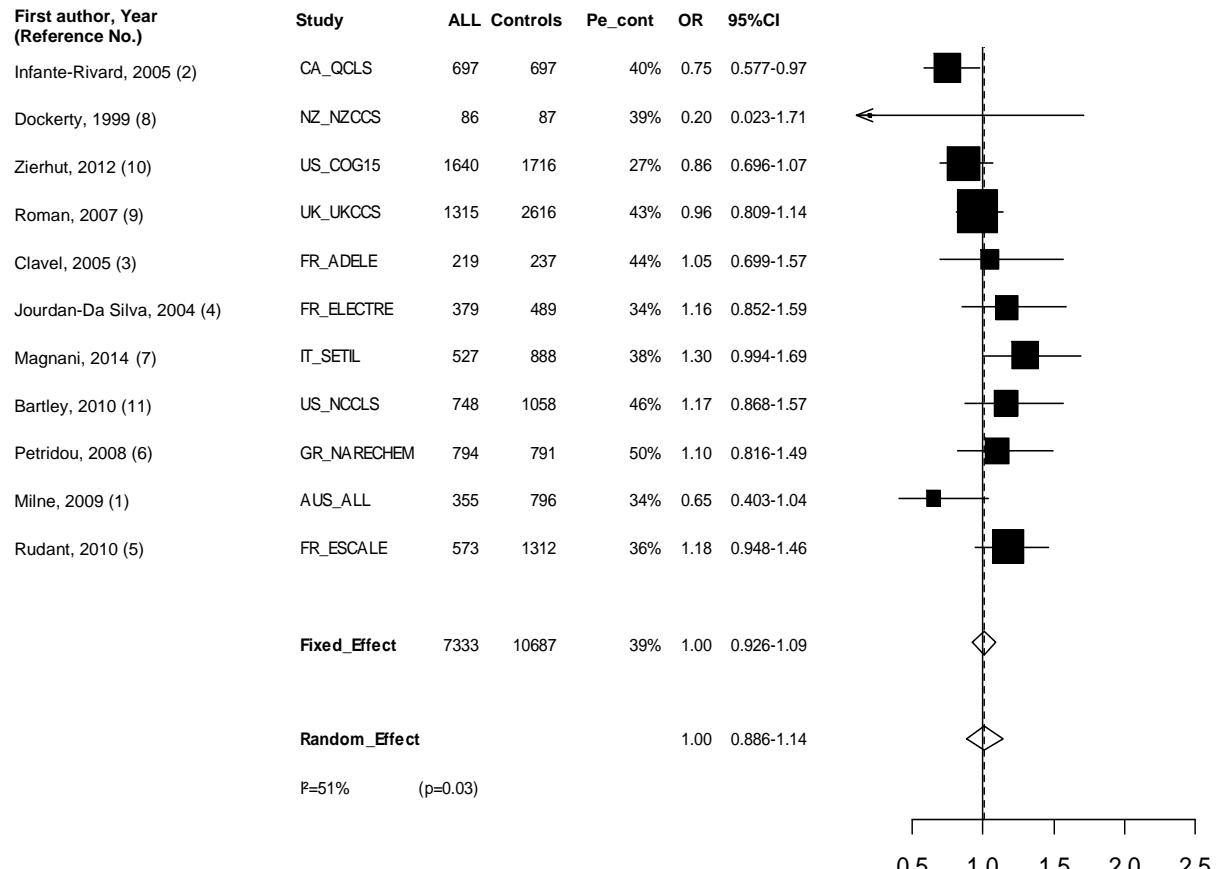
Study-specific OR and 95%CI were estimated by conditional (CA\_QCLS, GR\_NARECHEM, NZ\_NZCCS, US\_COG15, UK\_UKCCS) or unconditional (AUS\_ALL, FR\_ADELE, FR\_ELECTRE, FR\_ESCALE, IT\_SETIL, US\_NCCLS) logistic models, adjusted for age, gender, maternal educational level (AUS\_ALL, GR\_NARECHEM, FR\_ELECTRE, UK\_UKCCS, US\_COG15, US\_NCCLS), ethnicity (FR\_ADELE, US\_COG15, US\_NCCLS), region or center of recruitment (FR\_ADELE, UK\_UKCCS), region or state of residence (AUS\_ALL, FR\_ELECTRE), "urban/rural" status of the place of residence (GR\_NARECHEM), parental professional category (FR\_ESCALE), household income (US\_NCCLS), maternal age at child's birth (US\_NCCLS).

ALL: acute lymphoblastic leukemia, CI: confidence interval, OR: odds ratios; Pe\_cont: prevalence of exposure among controls; AUS\_ALL: Australian study of causes of acute lymphoblastic leukaemia in children; CA\_QCLS: Quebec childhood leukemia study (Canada); FR\_ADELE: Adele study (France); FR\_ELECTRE: Electre study (France); FR\_ESCALE: Epidemiological study on childhood cancer and leukemia (France); GR\_NARECHEM: Nationwide registration for childhood haematological malignancies (Greece); IT\_SETIL: Study on the etiology of childhood lymphohematopoietic malignancies (Italy); NZ\_NZCCS: New Zealand childhood cancer study; UK\_UKCCS: United Kingdom childhood cancer study; US\_COG15: Children's oncology group study (US); US\_NCCLS: Northern California childhood leukemia study (US).

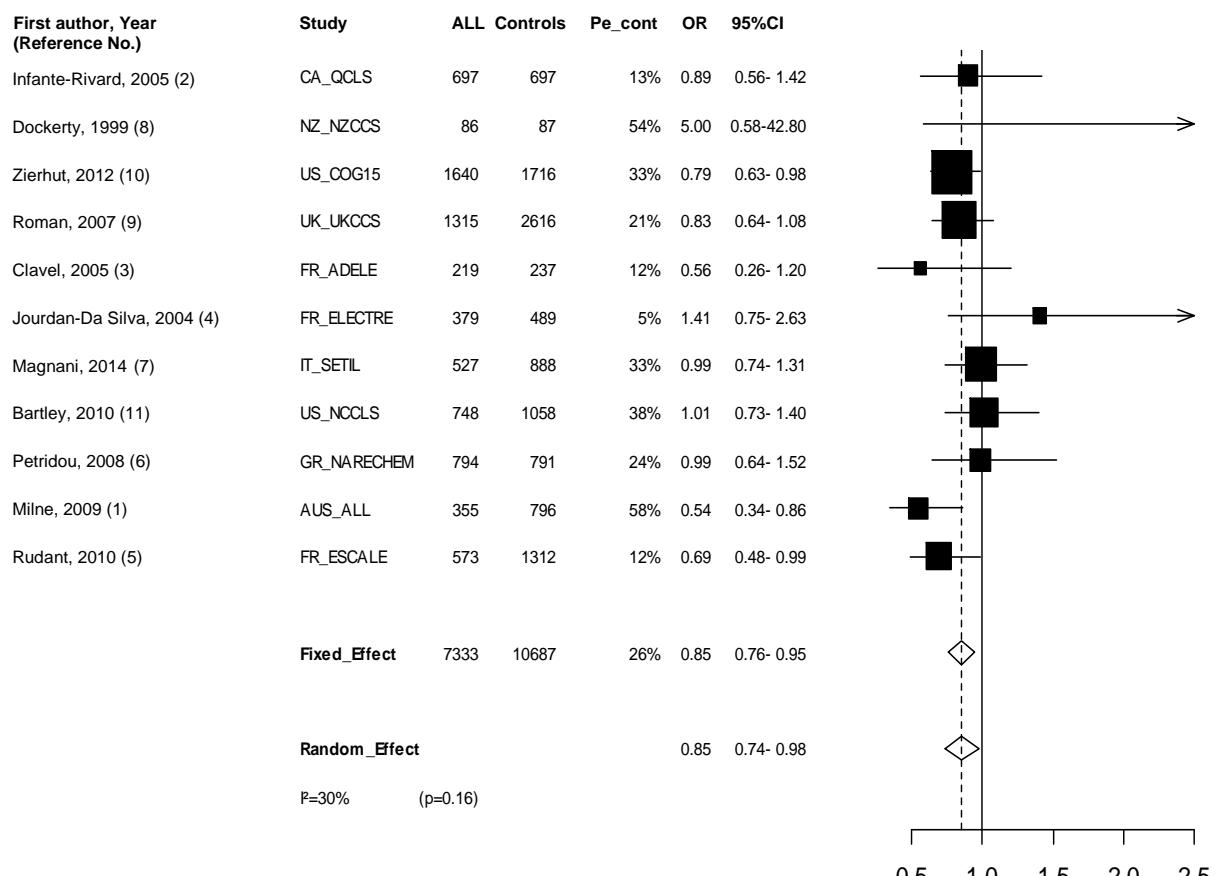
### Breastfeeding, yes vs. no



### Breastfeeding, < 6 months vs. never breastfed



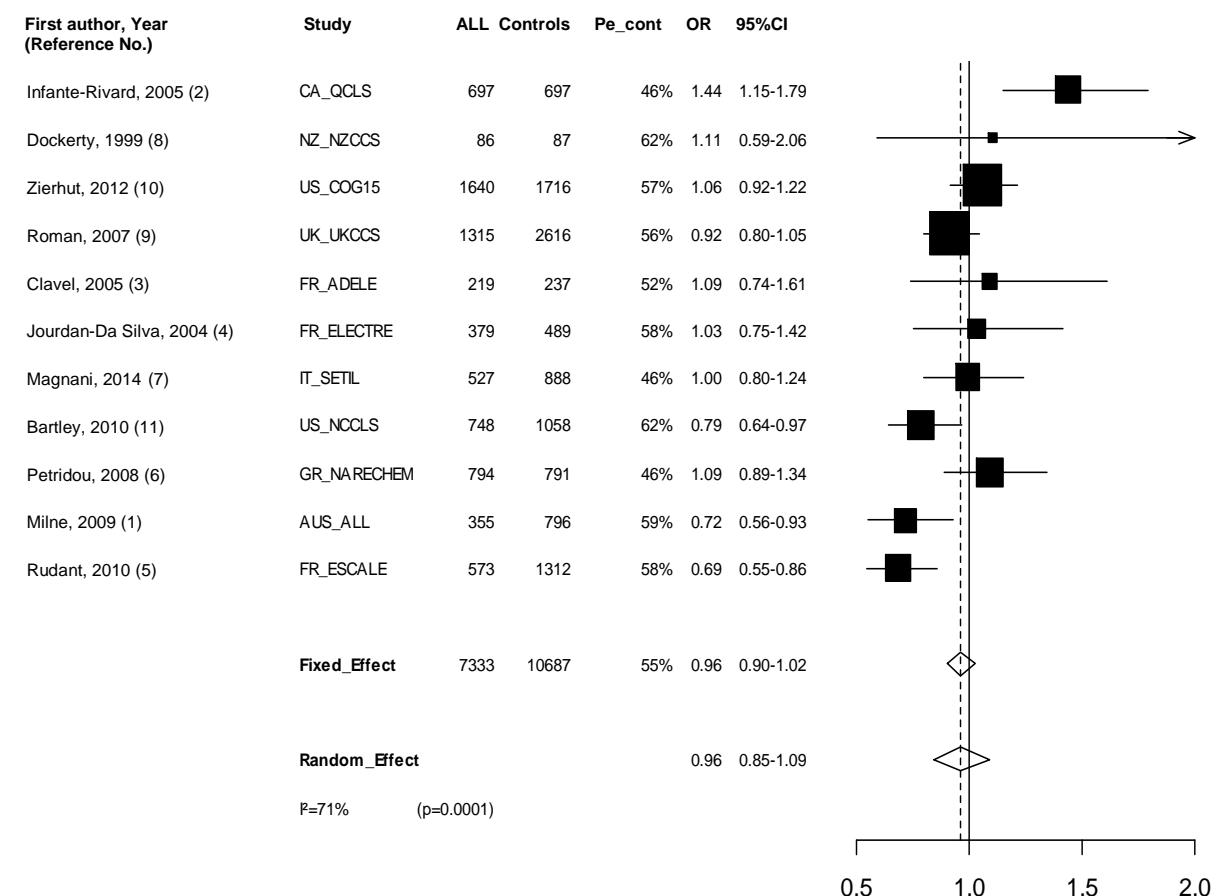
### Breastfeeding, ≥ 6 months vs. never breastfed



**Web Figure 2. Association between ALL and birth order (2 and more vs. first born)**, restriction to children aged  $\geq$  2 years, meta-analysis of 11 studies, Childhood Leukemia International Consortium. Studies are ordered by increasing study period.

Study-specific OR and 95%CI were estimated by conditional (CA\_QCLS, GR\_NARECHEM, NZ\_NZCCS, US\_COG15, UK\_UKCCS) or unconditional (AUS\_ALL, FR\_ADELE, FR\_ELECTRE, FR\_ESCALE, IT\_SETIL, US\_NCCLS) logistic models, adjusted for age, gender, maternal educational level (AUS\_ALL, GR\_NARECHEM, IT\_SETIL, UK\_UKCCS, US\_COG15, US\_NCCLS), ethnicity (FR\_ADELE, US\_NCCLS), region or center of recruitment (FR\_ADELE, UK\_UKCCS), region or state of residence (AUS\_ALL, FR\_ELECTRE), parental professional category (FR\_ESCALE), maternal age at child's birth (FR\_ELECTRE, FR\_ESCALE, US\_NCCLS).

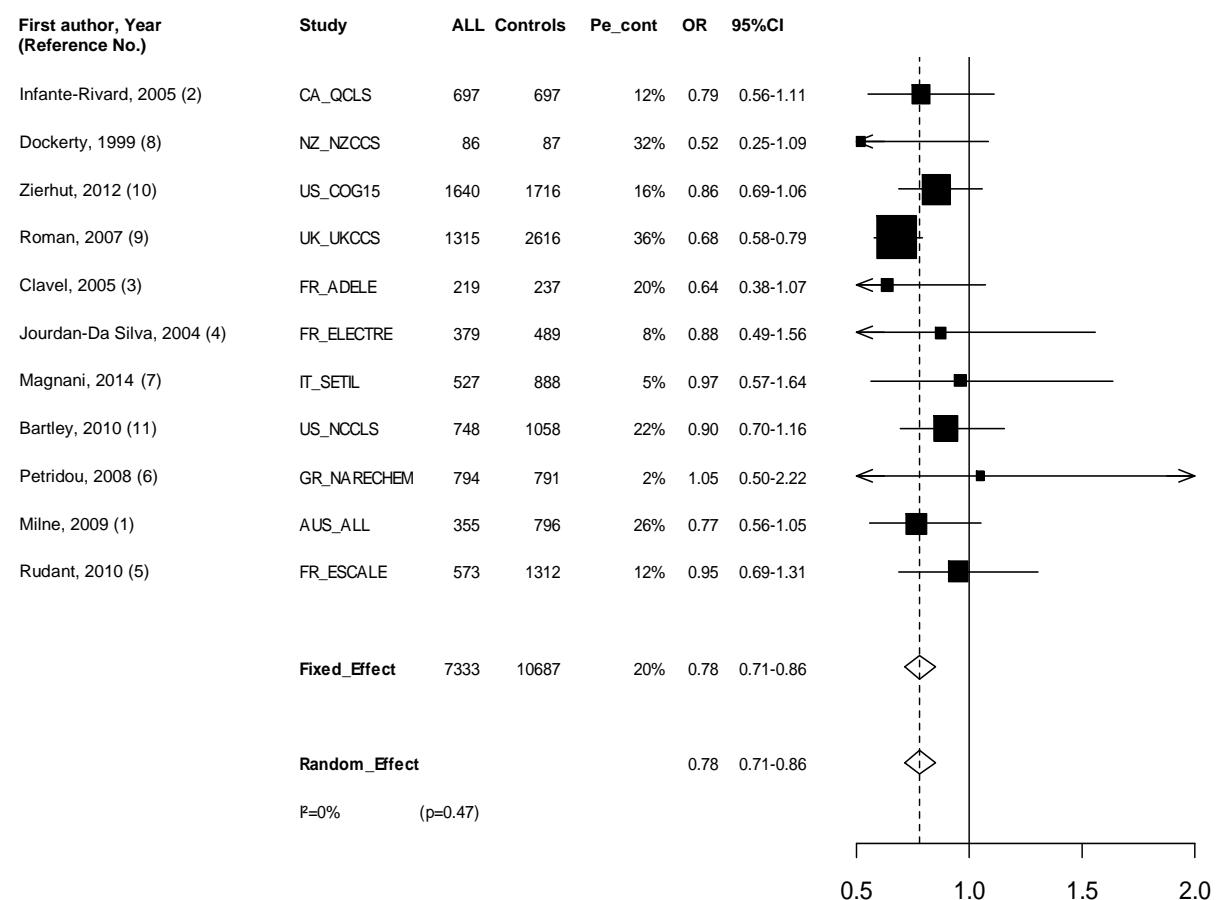
ALL: acute lymphoblastic leukemia, CI: confidence interval, OR: odds ratios; Pe\_cont: prevalence of exposure among controls; AUS\_ALL: Australian study of causes of acute lymphoblastic leukaemia in children; CA\_QCLS: Quebec childhood leukemia study (Canada); FR\_ADELE: Adele study (France); FR\_ELECTRE: Electre study (France); FR\_ESCALE: Epidemiological study on childhood cancer and leukemia (France); GR\_NARECHEM: Nationwide registration for childhood haematological malignancies (Greece); IT\_SETIL: Study on the etiology of childhood lymphohematopoietic malignancies (Italy); NZ\_NZCCS: New Zealand childhood cancer study; UK\_UKCCS: United Kingdom childhood cancer study; US\_COG15: Children's oncology group study (US); US\_NCCLS: Northern California childhood leukemia study (US).



**Web Figure 3. Association between ALL and day-care center attendance in the first year of life (yes vs. no), restriction to children aged  $\geq$  2 years, meta-analysis of 11 studies, Childhood Leukemia International Consortium. Studies are ordered by increasing study period.**

Study-specific OR and 95%CI were estimated by conditional (CA\_QCLS, GR\_NARECHEM, NZ\_NZCCS, US\_COG15, UK\_UKCCS) or unconditional (AUS\_ALL, FR\_ADELE, FR\_ELECTRE, FR\_ESCALE, IT\_SETIL, US\_NCCLS) logistic models, adjusted for age, gender, maternal educational level (AUS\_ALL, FR\_ELECTRE, UK\_UKCCS, US\_COG15, US\_NCCLS), ethnicity (FR\_ADELE, US\_NCCLS), region or center of recruitment (FR\_ADELE, UK\_UKCCS), region or state of residence (AUS\_ALL, FR\_ELECTRE), parental professional category (FR\_ESCALE), maternal age at child's birth (FR\_ELECTRE, US\_NCCLS).

ALL: acute lymphoblastic leukemia, CI: confidence interval, OR: odds ratios; Pe\_cont: prevalence of exposure among controls; AUS\_ALL: Australian study of causes of acute lymphoblastic leukaemia in children; CA\_QCLS: Quebec childhood leukemia study (Canada); FR\_ADELE: Adele study (France); FR\_ELECTRE: Electre study (France); FR\_ESCALE: Epidemiological study on childhood cancer and leukemia (France); GR\_NARECHEM: Nationwide registration for childhood haematological malignancies (Greece); IT\_SETIL: Study on the etiology of childhood lymphohematopoietic malignancies (Italy); NZ\_NZCCS: New Zealand childhood cancer study; UK\_UKCCS: United Kingdom childhood cancer study; US\_COG15: Children's oncology group study (US); US\_NCCLS: Northern California childhood leukemia study (US).



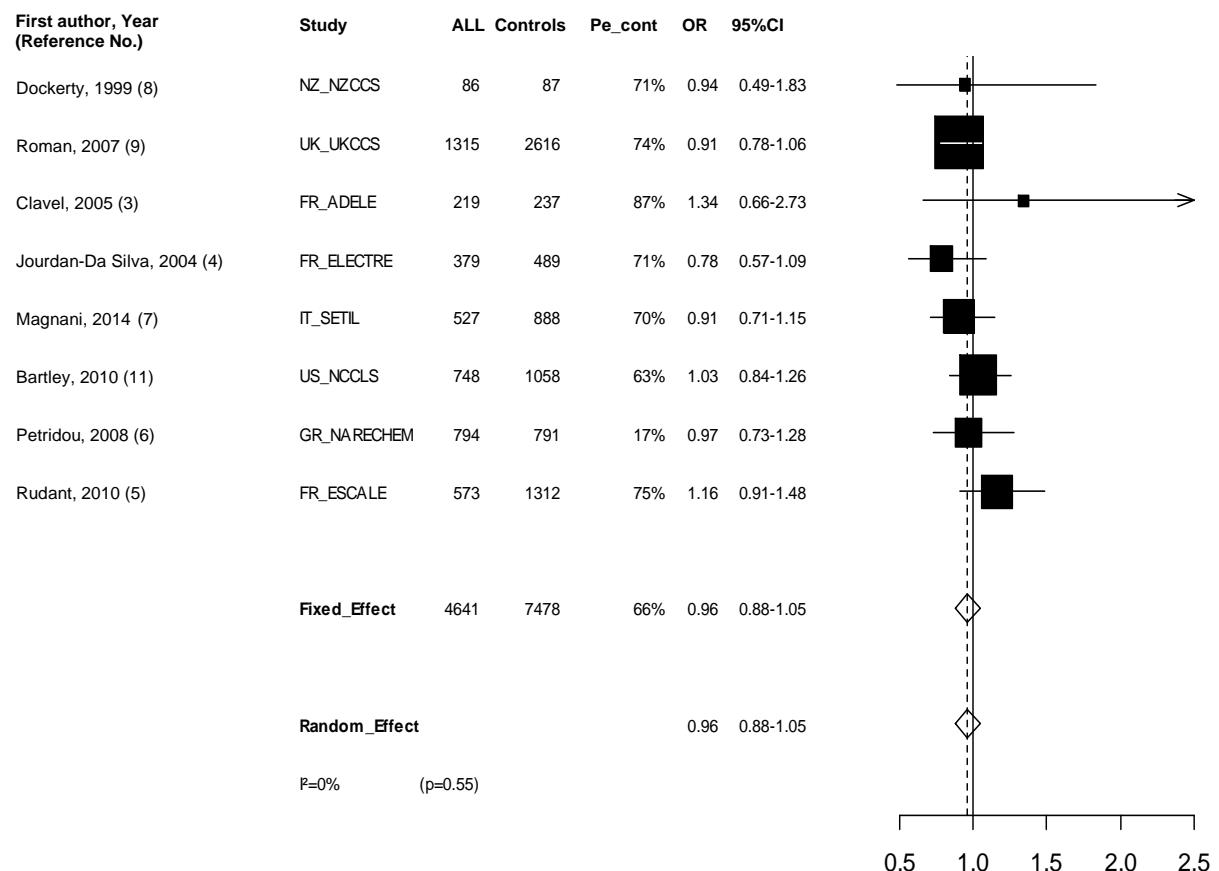
**Web Figure 4. Association between ALL and history of common infections in the first year of life**, restriction to children aged  $\geq 2$  years, meta-analysis of 8 studies, Childhood Leukemia International Consortium. Studies are ordered by increasing study period.

Study-specific OR and 95%CI were estimated by conditional (GR\_NARECHEM, NZ\_NZCCS, UK\_UKCCS) or unconditional (FR\_ADELE, FR\_ELECTRE, FR\_ESCALE, IT\_SETIL, US\_NCCLS) logistic models, adjusted for age, gender, maternal educational level (FR\_ELECTRE, UK\_UKCCS), ethnicity (FR\_ADELE, US\_NCCLS), region or center of recruitment (FR\_ADELE, UK\_UKCCS), region or state of residence (FR\_ELECTRE), parental professional category (FR\_ESCALE), maternal age at child's birth (US\_NCCLS).

Four or more episodes was defined as 4 or more episodes of any common infection in the 4 studies that had provided the total number of episodes (GR\_NARECHEM, IT\_SETIL, UK\_UKCCS, US\_NCCLS), and by 4 or more episodes of infection at a particular site or 1–3 episodes of infection of a minimum of 4 sites occurring in infancy, for the 3 French studies (FR\_ADELE, FR\_ELECTRE, FR\_ESCALE).

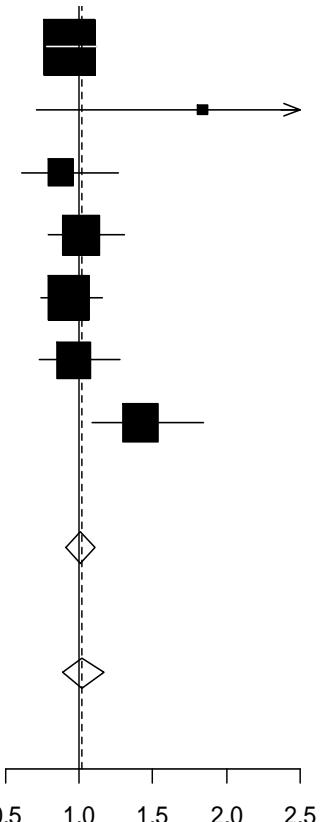
ALL: acute lymphoblastic leukemia, CI: confidence interval, OR: odds ratios; Pe\_cont: prevalence of exposure among controls; FR\_ADELE: Adele study (France); FR\_ELECTRE: Electre study (France); FR\_ESCALE: Epidemiological study on childhood cancer and leukemia (France); GR\_NARECHEM: Nationwide registration for childhood haematological malignancies (Greece); IT\_SETIL: Study on the etiology of childhood lymphohematopoietic malignancies (Italy); NZ\_NZCCS: New Zealand childhood cancer study; UK\_UKCCS: United Kingdom childhood cancer study; US\_NCCLS: Northern California childhood leukemia study (US).

#### History of common infections, at least one vs. none



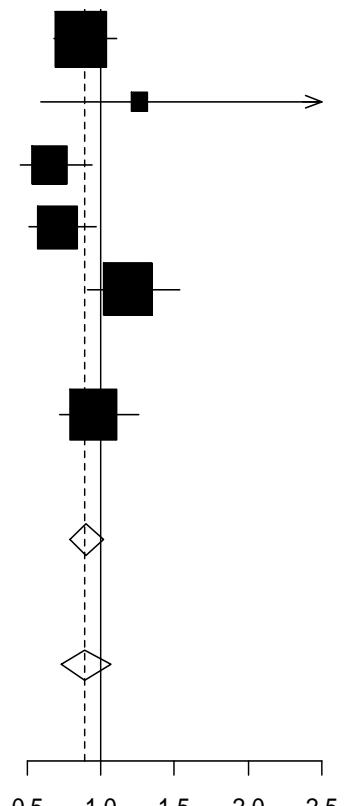
### History of common infections, 1 to 3 vs. none

First author, Year (Reference No.)	Study	ALL	Controls	Pe_cont	OR	95%CI
Roman, 2007 (9)	UK_UKCCS	1315	2616	49%	0.94	0.79-1.12
Clavel, 2005 (3)	FR_ADELE	219	237	43%	1.84	0.71-4.72
Jourdan-Da Silva, 2004 (4)	FR_ELECTRE	379	489	33%	0.88	0.61-1.26
Magnani, 2014 (7)	IT_SETIL	527	888	46%	1.01	0.79-1.31
Bartley, 2010 (11)	US_NCCLS	748	1058	43%	0.93	0.74-1.16
Petridou, 2008 (6)	GR_NARECHEM	794	791	17%	0.97	0.73-1.28
Rudant, 2010 (5)	FR_ESCALE	573	1312	38%	1.42	1.09-1.85
<b>Fixed_Effect</b>		7333	10687	41%	1.01	0.91-1.11
<b>Random_Effect</b>				1.02	0.89-1.17	
I <sup>2</sup> =38% (p=0.14)						



### History of common infections, 4 or more vs. none

First author, Year (Reference No.)	Study	ALL	Controls	Pe_cont	OR	95%CI
Roman, 2007 (9)	UK_UKCCS	1315	2616	25%	0.86	0.68-1.11
Clavel, 2005 (3)	FR_ADELE	219	237	43%	1.26	0.59-2.71
Jourdan-Da Silva, 2004 (4)	FR_ELECTRE	379	489	35%	0.65	0.45-0.94
Magnani, 2014 (7)	IT_SETIL	527	888	24%	0.71	0.51-0.97
Bartley, 2010 (11)	US_NCCLS	748	1058	20%	1.18	0.91-1.54
Petridou, 2008 (6)	GR_NARECHEM	794	791	0%		
Rudant, 2010 (5)	FR_ESCALE	573	1312	37%	0.95	0.72-1.26
<b>Fixed_Effect</b>		4555	7391	25%	0.90	0.79-1.02
<b>Random_Effect</b>				0.89	0.73-1.07	
I <sup>2</sup> =52% (p=0.07)						

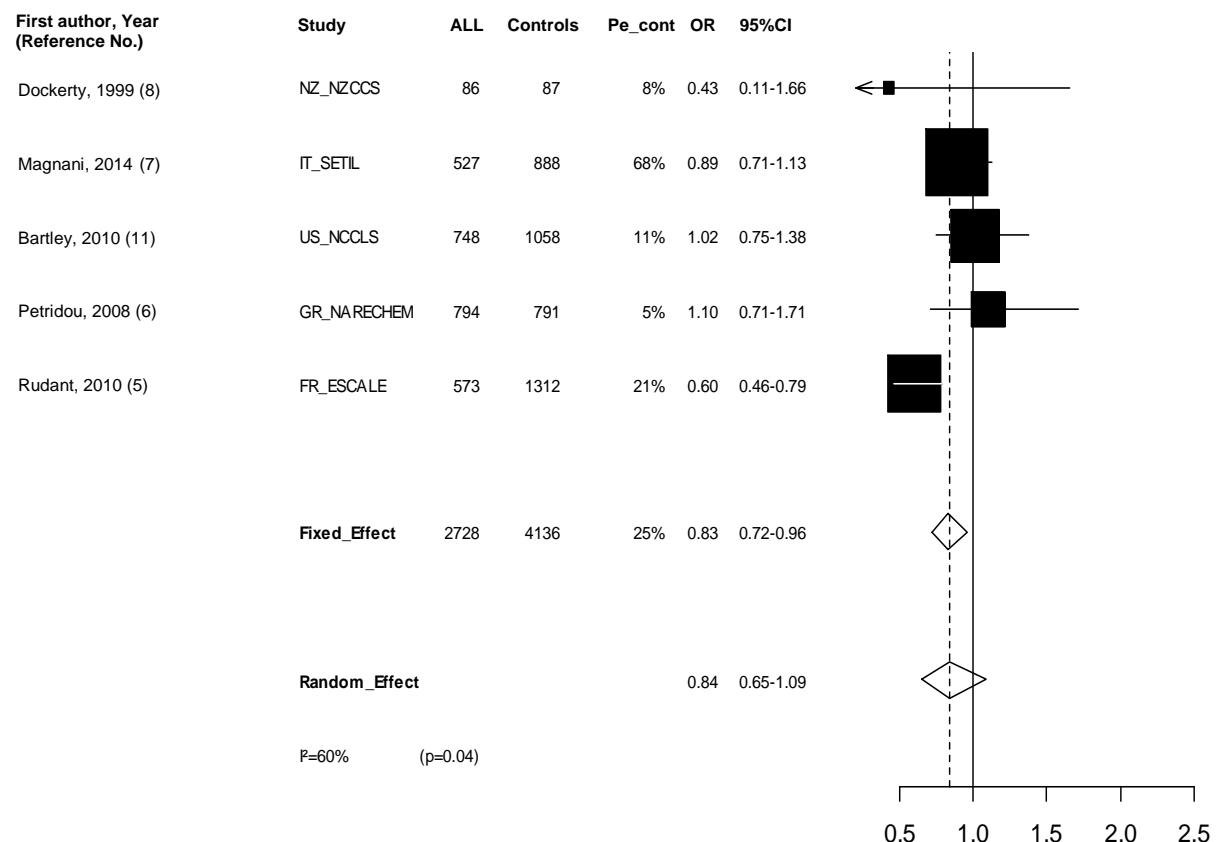


**Web Figure 5. Association between ALL and history of lower respiratory tract infections in the first year of life**, restriction to children aged  $\geq 2$  years, meta-analysis of 5 studies, Childhood Leukemia International Consortium. Studies are ordered by increasing study period.

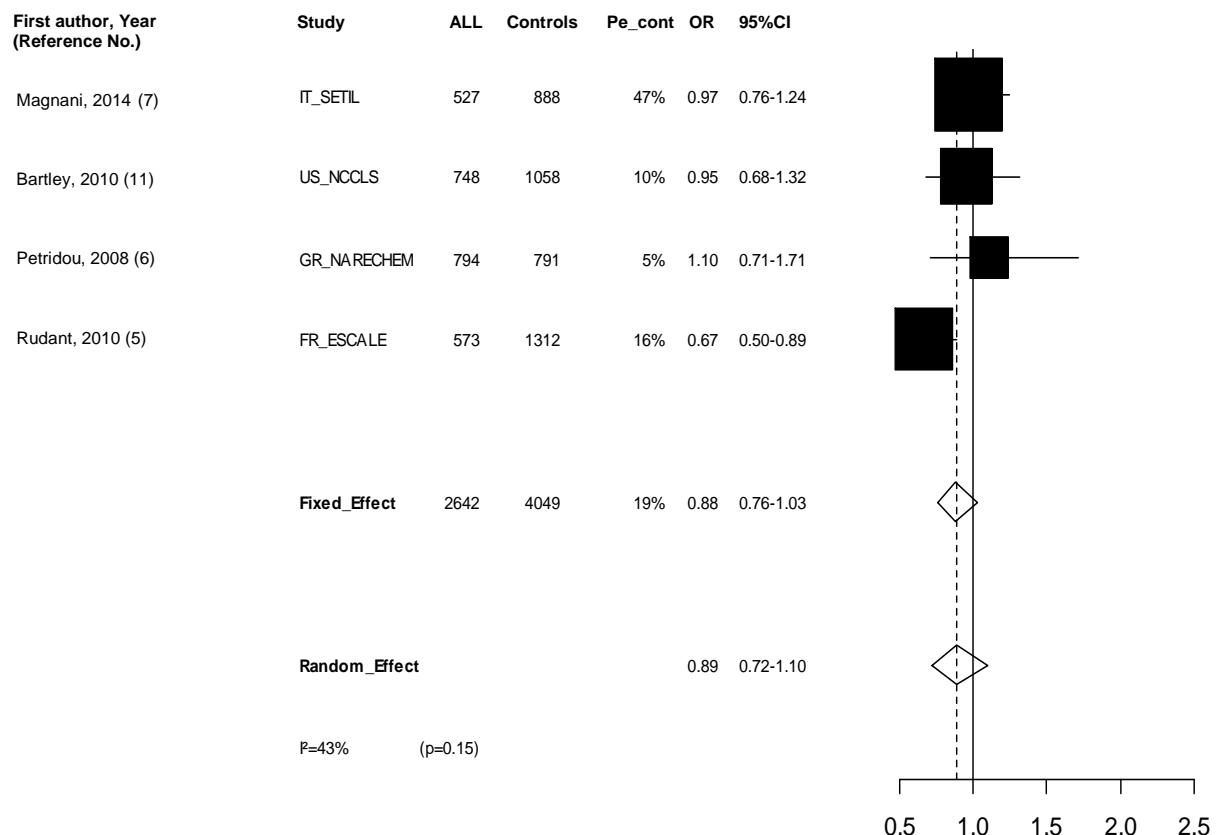
Study-specific OR and 95%CI were estimated by conditional (GR\_NARECHEM, NZ\_NZCCS) or unconditional (FR\_ESCALE, IT\_SETIL, US\_NCCLS) logistic models, adjusted for age, gender, ethnicity (US\_NCCLS), parental professional category (FR\_ESCALE), maternal age at child's birth (US\_NCCLS).

ALL: acute lymphoblastic leukemia, CI: confidence interval, OR: odds ratios; Pe\_cont: prevalence of exposure among controls; FR\_ESCALE: Epidemiological study on childhood cancer and leukemia (France); GR\_NARECHEM: Nationwide registration for childhood haematological malignancies (Greece); IT\_SETIL: Study on the etiology of childhood lymphohematopoietic malignancies (Italy); NZ\_NZCCS: New Zealand childhood cancer study; US\_NCCLS: Northern California childhood leukemia study (US).

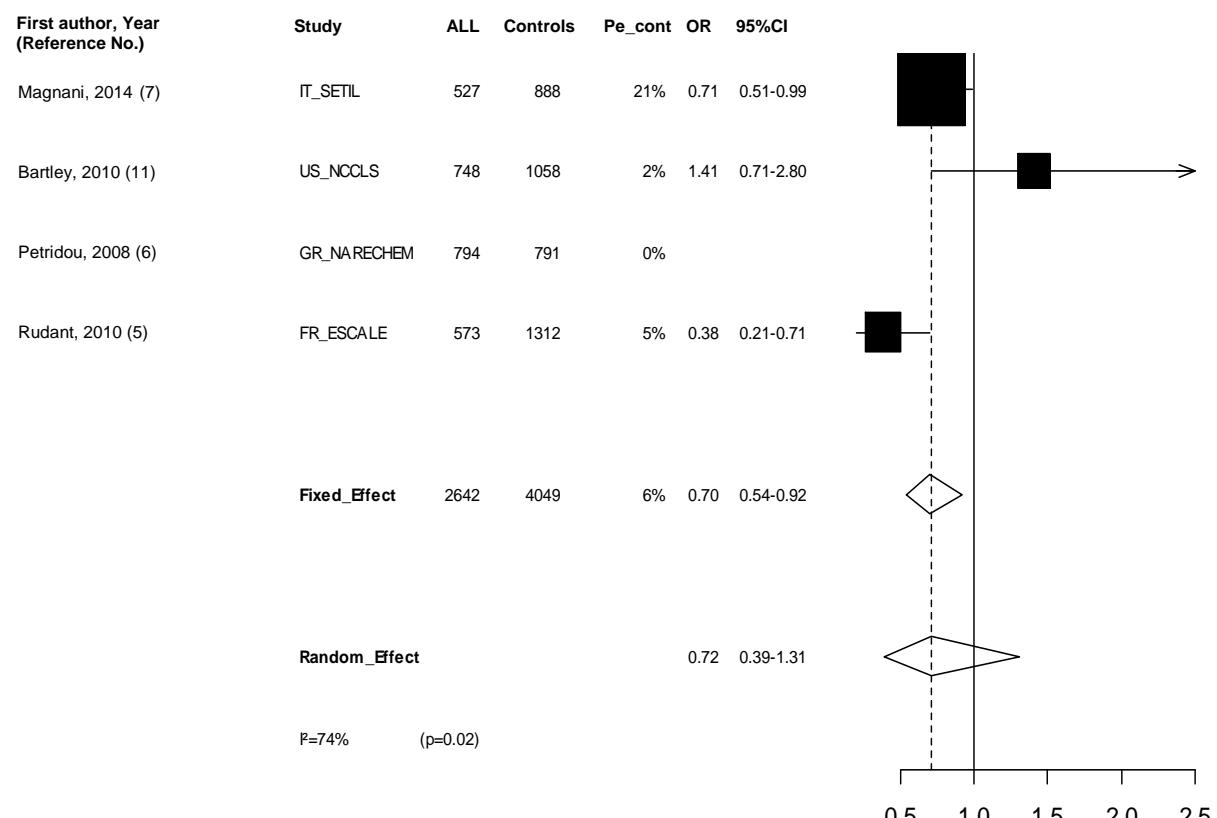
### History of lower respiratory tract infections, at least one vs. none



### History of lower respiratory tract infections, 1 to 3 vs. none



### History of lower respiratory tract infections, 4 or more vs. none



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